Appl. No. 10/699,562 Amdt. dated August 13, 2007 Amendment under 37 CFR 1.116 Expedited Procedure Examining Group 1618

## **Listing of the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

1	1 (previously presented): A molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$ , wherein
2	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
3	suitable for cellular uptake,
4	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
5	when linked with portion $\mathbf{B}$ is effective to inhibit or prevent cellular uptake of portion $\mathbf{B}$ , and
6	X is a linker of about 2 to about 100 atoms joining A with B, which can be
7	cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID NO: 1.
1	2 (original): The molecule of claim 1, wherein said peptide portion A comprises
2	about 5 to about 9 glutamates or aspartates.
1	3 (original): The molecule of claim 2, wherein said peptide portion A comprises
2	about 5 to about 9 consecutive glutamates or aspartates.
1	4 (original): The molecule of claim 1, wherein said peptide portion <b>B</b> comprises
2	about 9 to about 16 arginines.
1	5 (original): The molecule of claim 4, wherein said peptide portion B comprises
2	about 9 to about 16 consecutive arginines.
1	6 (original): The molecule of claim 1, wherein said peptide portion A comprises
2	D-amino acids.
1	7 (original): The molecule of claim 1, wherein said peptide portion <b>B</b> comprises
2	D-amino acids.

1	8 (original): The molecule of claim 1, wherein said peptide portion A consists of
2	D-amino acids.
1	9 (original): The molecule of claim 1, wherein said peptide portion <b>B</b> consists of
2	D-amino acids.
1	10 (original): The molecule of claim 1, wherein said peptide portions A and B
2	consists of D-amino acids.
1	11 (previously presented): A molecule for transporting a cargo moiety across a
2	cell membrane of the structure $A - X - B - C$ , wherein
3	C is a portion comprising a cargo moiety,
4	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
5	suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance
6	transport of cargo portion C across a cell membrane,
7	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
8	when linked with portion ${\bf B}$ is effective to inhibit or prevent cellular uptake of ${\bf B}$ - ${\bf C}$ , and
9	<b>X</b> is a cleavable linker of about 2 to about 100 atoms joining <b>A</b> with $\mathbf{B} - \mathbf{C}$ , which
10	can be cleaved under physiological conditions, wherein $\mathbf{X}$ comprises the sequence of SEQ ID
11	NO: <u>1</u> .
1	12 (original): The molecule of claim 11, wherein said peptide portion A
2	comprises amino acids selected from the group of acidic amino acids consisting of glutamate and
3	aspartate.
1	13 (original): The molecule of claim 11, wherein said peptide portion <b>B</b>
2	comprises amino acids selected from the group of basic amino acids consisting of arginine and
3	histidine.
1	14 (original): The molecule of claim 11, wherein said cargo portion C is selected
2	from the group of cargo moieties consisting of a fluorescent moiety, a fluorescence-quenching

- 3 moiety, a radioactive moiety, a radiopaque moiety, a paramagnetic moiety, a nanoparticle, a 4 vesicle, a molecular beacon, a marker, a marker enzyme, a contrast agent, a chemotherapeutic 5 agent, and a radiation-sensitizer. 1 15 (original): The molecule of claim 14, wherein the cargo portion C comprises 2 a contrast agent for diagnostic imaging. 1 16 (original): The molecule of claim 14, wherein the cargo portion C comprises 2 a radiation sensitizer for radiation therapy. 1 17 (original): The molecule of claim 11, wherein said peptide portion A 2 comprises about 5 to about 9 glutamates or aspartates. 1 18 (original): The molecule of claim 17, wherein said peptide portion A 2 comprises about 5 to about 9 consecutive glutamates or aspartates. 1 19 (original): The molecule of claim 11, wherein said portion peptide **B** 2 comprises between about 9 to about 16 arginines. 1 20 (original): The molecule of claim 19, wherein said peptide portion **B** 2 comprises between about 9 to about 16 consecutive arginines. 1 21 (original): The molecule of claim 11, wherein said peptide portion A 2 comprises D-amino acids. 1 22 (original): The molecule of claim 11, wherein said peptide portion **B** 2 comprises D-amino acids.
- 1 23 (original): The molecule of claim 11, wherein said peptide portion A consists 2 of D-amino acids.
- 1 24 (original): The molecule of claim 11, wherein said peptide portion **B** consists 2 of D-amino acids.

1	25 (original): The molecule of claim 11, wherein said peptide portions A and B
2	consist of D-amino acids.
1	26 (original): The molecule of claim 25, wherein said peptide portion <b>B</b> consists
2	of D-arginine amino acids.
1	27 (original): The molecule of claim 11, wherein said peptide portion A is
2	located at a terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$ .
1	28 (original): The molecule of claim 11, wherein said peptide portion A is
2	located at the amino terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$ .
1	29 (original): The molecule of claim 11, wherein said peptide portion A is linked
2	near to or at the amino terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$ .
1	30 (original): The molecule of claim 11, wherein said peptide portion A is linked
2	near to or at the carboxy terminus of a polypeptide chain comprising $\mathbf{B} - \mathbf{C}$ .
1	31 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide
2	chain having ends consisting of a B-side terminus and a C-side terminus, and wherein cleavable
3	linker X is disposed near or at said B-side terminus.
1	32 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide
2	chain having ends consisting of a B-side terminus and a C-side terminus, and wherein cleavable
3	linker X is disposed near or at said C-side terminus.
	33-36 (canceled)
l	37 (original): The molecule of claim 11, wherein cleavable linker X comprises
2	aminocaproic acid.
	38-44 (canceled)

1	45 (original): The molecule of claim 11, comprising a plurality of cleavable
2	linkers $X$ linking a portion $A$ to a structure $B - C$ .
1	46 (previously presented): A pharmaceutical composition comprising:
2	A molecule of the structure $A - X - B$ , wherein
3	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
4	suitable for cellular uptake,
5	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
6	when linked with portion $\bf B$ is effective to inhibit or prevent cellular uptake of portion $\bf B$ , and
7	X is a cleavable linker of about 3 to about 30 atoms joining $A$ with $B$ , which can
8	be cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID NO: 1;
9	and
10	a pharmaceutically acceptable carrier.
1	47 (previously presented): The pharmaceutical composition of claim 46, wherein
2	said portion A has between about 5 to about 9 acidic amino acid residues, and said
3	portion <b>B</b> has between about 9 to about 16 basic amino acid residues.
1	48 (original): The pharmaceutical composition of claim 46 or 47, further
2	comprising a portion C covalently attached to said portion B and comprising a cargo moiety.
1	49 (withdrawn): A method of modulating cellular uptake of a peptide <b>B</b> of about
2	5 to about 20 basic amino acid residues, which is suitable for cellular uptake, comprising:
3	linking said peptide ${\bf B}$ to a peptide ${\bf A}$ of about 2 to about 20 acidic amino acid
4	residues with a cleavable linker $\mathbf{X}$ of about 3 to about 30 atoms, which can be cleaved under
5	physiological conditions and
6	cleaving said cleavable linker $X$ effective to separate peptide $B$ from molecule $A$ .
1	50 (withdrawn): A method of modulating cellular uptake of a cargo moiety C,
2	comprising:

3	covalently attaching a cargo moiety C to a peptide B of about 5 to about 20 basic
4	amino acid residues to form a molecule $\mathbf{B} - \mathbf{C}$ ;
5	linking said molecule $\mathbf{B} - \mathbf{C}$ to a peptide $\mathbf{A}$ of about 2 to about 20 acidic amino
6	acid residues with a cleavable linker X of about 3 to about 30 atoms, and
7	cleaving said cleavable linker $X$ effective to separate $B-C$ from said peptide $A$ .
1	51 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$ ,
2	wherein
3	B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
4	for cellular uptake,
5	A is a peptide of about 2 to about 20 acidic amino acid residues, which when
6	linked with peptide $\bf B$ is effective to inhibit or prevent cellular uptake of peptide $\bf B$ , and
7	X is a cleavable linker portion of between 1 and 10 amino acid residues joining A
8	with B, which can be cleaved under physiological conditions.
1	52 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$
2	C, wherein
3	C is a peptide cargo moiety,
4	B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
5	for cellular uptake,
6	A is a peptide of about 2 to about 20 acidic amino acid residues, which when
7	linked with peptide $\bf B$ is effective to inhibit or prevent cellular uptake of peptide $\bf B - C$ , and
8	X is a cleavable linker portion of between 1 and 10 amino acid residues joining A
9	with $\mathbf{B} - \mathbf{C}$ which can be cleaved under physiological conditions.
1	53 (withdrawn): A molecule for transporting a fluorescent cargo moiety across a
2	cell membrane of the structure $\mathbf{Q} - \mathbf{A} - \mathbf{X} - \mathbf{B} - \mathbf{C}$ , wherein
3	C is a portion comprising a fluorescent cargo moiety,

4	<b>B</b> is a peptide portion of about 5 to about 20 basic amino acid residues, which is
5	suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance
6	transport of cargo portion C across a cell membrane,
7	${f Q}$ is a quencher moiety attached to ${f A}$ and effective to quench fluorescence from
8	fluorescent cargo C;
9	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
10	when linked with portion $\bf B$ is effective to inhibit or prevent cellular uptake of $\bf B - C$ , and
11	<b>X</b> is a cleavable linker of about 2 to about 100 atoms joining <b>A</b> with $\mathbf{B} - \mathbf{C}$ , which
12	can be cleaved under physiological conditions.

## 54 -55 (canceled)

56 (original): The molecule of claim 11, comprising a single cargo portion **C** linked to a plurality of portions **B**, each of portions **B** being linked to a cleavable linker portion **X** linked to an acidic portion **A**.